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Effect of the mother's consumption of traditional Chinese herbs on estimated infant daily intake of lead from breast milk

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Abstract

Infant exposure to lead through breast milk is of special concern because breast milk is considered the best food source for infants under 6 months. In this study, a total of the mothers provided colostrum samples once in the early postpartum period, but only 16 of them provided breast milk weekly at 1–60 days postpartum. The geometric mean of lead concentrations in all colostrum samples (n=72) was 7.68±8.24 μg/L. The concentration of lead in the breast milk of the consumption group (the mothers who consumed traditional Chinese herbs) was 8.59±10.95 μg/L, a level significantly higher than the level of 6.84±2.68 μg/L found in the control group (mothers who did not consume traditional Chinese herbs). In the consumption group (n=9), the mean concentration of lead in the breast milk decreased with days postpartum, from 9.94 μg/L in colostrum to 2.34 μg/L in mature milk. We found the highest daily lead intake in infants at birth, and the level gradually decreased after the first month. We used an estimation of the hazard index (HI) to analyze the health risk of infants. In total, 5.7% (2 out of 35) of the HI estimates exceed 1.0 for the consumption group. In conclusion, the consumptions of traditional Chinese herbs by the mothers in this study significantly affected the body burden of lead in their infants.

Keywords: Breast milk; Traditional Chinese herbs; Daily lead intake; Hazard index

1. Introduction

Traditional Chinese herbs have been used in Chinese society for thousands of years, and consequently many husbands and family members would like to use herbal remedies to keep pregnant women in

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good health. However, increasing numbers of cases of heavy metal (such as lead (Pb), arsenic (As), and mercury (Hg)) intoxication caused by traditional Chinese herbs have been reported (Chan et al., 1977; Lightfoote et al., 1977; Baker et al., 1985; Huxtable, 1990; Chan et al., 1993; Markowitz et al., 1994). For example, in Taiwan, a 5-month-old baby girl died due to long-term consumption of traditional Chinese herbs, Ba-Pao-NeHwang-San, with a lead level of 44,000 ppm (Chi et al., 1993). There also have been reports of Ayurvedic medications causing lead poisoning in children because of their contamination with lead. Traditional Chinese herbs may be harvested from contaminated soil, so contaminants of herbs can be responsible for unexpected toxicity (But, 1994). These cases have drawn public attention to the regulation and safety of traditional Chinese herbs. However, according to our best knowledge, there are only a few officially recommended upper limits to the levels of heavy metals in traditional Chinese herbs in the world (Uen, 1999).

Lead is neurotoxic and may cause mental deficiency, movement disorders, kidney dysfunction, and abnormal perception, especially during fetal growth and development. Recent studies indicate that lead exposure during the first 3 years of life has the most long-lasting and damaging effects (Pueschel et al., 1996). At this stage, children's developing brains are most vulnerable to lead exposure because children of this age have a less well developed barrier between the blood and the brain, allowing relatively more lead to pass into their developing brains. Also, studies have suggested that lead itself acts to disrupt this barrier (Finkelstein et al., 1998).

Women are chronically exposed to environmental lead since infancy, and they accumulate a significant bone lead burden into the child-bearing age. Maternal body burden and current exposure are major lead sources for the fetus, because lead can pass through the placenta (Ellenhorn, 1997). Breast milk is the first food for infants and it serves as the major nutrient source for biological functions and growth during the early stages of life. There are some data on infant blood lead levels in relation to breast milk lead. Ryu et al. (1985) found a strong correlation between lead concentrations in the breast milk and the corresponding blood lead concentrations of infants until 6 months of age (r=0.42, p<0.0003), before infants begin to crawl and walk. In rats, Bogden et al. (1991) found that lead exposure during pregnancy could retard fetal growth and development, especially if the maternal diet during pregnancy was low in calcium. Gulson et al. (1998) assumed that there was no contribution from environmental samples such as house dust and ambient air. The contribution of lead in the breast milk as the only dietary source to the blood lead level of newborns was estimated from lead isotopic measurements to be in the range of 40–65% (Gulson et al., 1998). Therefore breast-feeding constitutes a major source of exposure to bioaccumulated contaminants for infants.

In Taiwan, little information is available on the association between consumption of traditional Chinese herbs and lead concentrations of breast milk. In this study, we examined the relationship between lead concentrations in breast milk and the consumption of traditional Chinese herbs commonly used during pregnancy and lactation. In order to assess the lead exposure in breastfeeding infants, we calculated and validated a hazard index to evaluate the impact of consumption of traditional Chinese herbs in infants in Taiwan.

2. Methods

2.1. Questionnaire collection

A total of 72 healthy mothers were recruited for the study. They were interviewed during pregnancy and lactation to collect information on their sociodemographic characteristics, residential environment, parity, obstetrical history, height and weight before and after pregnancy, occupational exposure history, and consumption of nutritional supplements, traditional Chinese herbs, alcohol, and tobacco. All of the mothers were served by the public water facility. None of the mothers had complications during the study period.

2.2. Collection and digestion of milk samples

Breast milk samples were collected from the subjects during the period from September 2001 to December 2003. All of the mothers provided colostrum samples once in the early postpartum period, but only 16 of them provided breast milk weekly at 1–60 days postpartum. Fifty milliliters of breast milk were collected each time using clean polyethylene bottles. Collected samples were shipped back to the laboratory immediately, freeze-dried, and then stored until analysis. Approximately 1 g of each sample was microwave digested (CEM, Model MDS-2000) with 4 mL nitric acid (Suprapur, Merck), 2 mL hydrogen peroxide (Suprapur, Merck) and 2 mL distilled water in closed Polyfluorotetraethylene (PFTE) vessels. After cooling, the residue fluid was diluted to 25 mL with distilled water.

2.3. Collection and digestion of traditional Chinese herbs

In individual questionnaires, we found that simple prescriptions, such as *Angelicae sinensis radix, Lycii fructus, Zizyphi fructu*, and Shy-Wuh-Tang were commonly consumed by mothers during pregnancy and lactation. Samples were purchased in sealed plastic bags directly from retail stores, traditional markets, and Chinese medicine clinics. Approximately 1 g of the herb or decoction was microwave digested with 15 ml nitric acid and 2 ml hydrogen peroxide in closed PFTE vessels. After cooling, the residue fluid was diluted to 100 mL with distilled water.

2.4. Lead analysis

Lead concentration was analyzed by Graphite atomic absorption spectrophotometry (GFAAS) (Varian, SpectrAA 220Z). Pd was a matrix modifier for lead. Certified reference material (CRM) BCR No. 151 milk powder and standard reference material (SRM) DORM-2 were used to perform a standard material test to ensure the precision and accuracy of the milk and herb analyses, respectively. The precision was 2.56% and 4.76% and the accuracy was 108.8% and 96.9%, respectively. The laboratory procedure recovery rates of lead were 107.7% and 97.3% for milk and herbs, respectively. We used 216 samples to determine the ratio of wet weight/dry weight for breast milk was 6.17±0.88 (mean±standard deviation). We divided the dry weight (μg/g) by 6.17 to calculate its corresponding wet weight (μg/L).

2.5. Estimating the half-life of lead in breast milk

To better evaluate the impact of nursing on infants, we used a first-order, one-compartment model to estimate the change of lead concentration in breast milk in the consumption group (who consumed traditional Chinese herbs) and the control group (who did not consume traditional Chinese herbs). The change of lead concentration in breast milk over time is assumed to follow the following first-order one-compartment model:

$$C_{\mathrm{m}}(t) = Ge^{-k_{\mathrm{m}}t}$$

where G and e are constant, k_{m} is the clearance rate constant of lead in breast milk (day^{-1}), $C_{\mathrm{m}}(t)$ is the time-dependent lead concentration in breast milk (μg/L).

2.6. Estimating daily intake and risk analysis

With consideration of appropriate ingestion rates, we divide two phases for estimating daily breast milk intakes. Firstly, the value for the daily energy requirement is approximately 80–120 kcal/day/kg for the first month of life. DHSS (1977) has examined expressed breast milk composition; the energy is 70 kcal/100 ml. The estimate intake amounts to 400–500 ml. Secondly, according Smith's study (1987), we assume the daily breast milk intakes remain relatively constant over an infant's life after the first month (760 ml/day). Typical weights of breastfeeding infants were obtained from WHO (1994).

The equation is:

$$\text{Daily intake} = \frac{\text{IR} \times C_{\mathrm{m}}(t)}{\text{BW}}$$

where IR=ingestion rate; $C_{\mathrm{m}}(t)$=lead concentration in breast milk (μg/L); BW=body weight (kg).

The methodology for estimating the hazard index (HI) was provided in USEPA Region risk-Based Concentration Table (USEPA, 2004), and used to analyze the health risk of infants. The HI was the ratio between the exposure and the reference dose.

The equation is:

$$\text{HI} = \frac{\text{IR} \times C_{\mathrm{m}}}{\text{RfD} \times \text{BW}_i}$$

where IR=ingestion rate; C_{m}=lead concentration in colostrum (μg/L); RfD=reference dose for infants(3.57 g/kg/day, FAO/WHO, 1989); BW_i=individual body weight. For non-carcinogenic effects, an HI exceeding 1.0 indicates that the infants who consumed the breast milk have potential health risk (USEPA, 2004).

2.7. Statistics

The distributions of continuous variables in the consumption and control groups were expressed as mean±standard deviation (SD). Age, height, weight, body mass index, and neonatal body weight among the two groups was examined by Student's *t*-test. The chi-square test was used to assess the independence of two categorical variables. For statistical analyses, right-skewed data were normalized by logarithmic transformation. We used Student's *t*-test to compare the breast milk lead concentrations between the consumption and control groups. Results were considered significant in a two-sided test if $p<0.05$.

3. Results

3.1. Lead concentrations in traditional Chinese herbs

The lead concentrations of four popular traditional Chinese herbs increased in the following order: *A. sinensis radix* (19.42±0.01 μg/kg)<*Z. fructus* (33.64±0.31 μg/kg)<*L. fructus* (36.76±0.01 μg/kg)<Shy-Wuh-Tang (322.31±0.30 μg/kg).

3.2. Demographic characteristics and lead concentrations in breast milk

Demographic characteristics of the 72 mothers and the smaller group who were actually followed over time are summarized and in Table 1. Mean body mass indices (BMI) after pregnancy are 25.5±3.81 and 27.0±2.67 kg/m^2 for the consumption group and control group, respectively. All of the mothers did not have occupational exposure and only very few of them (<1%) consumed cigarettes and alcohol during pregnancy. Fig. 1 shows box and whisker plots of colostrum lead concentrations. The geometric mean of lead concentration in all colostrum samples (n=72) is 7.68±8.24 μg/L. The breast milk lead concentration of the consumption group (8.59±10.95 μg/L) is statistically significantly higher than for the control group (6.84±2.68 μg/L) ($p<0.05$).

3.3. Half-life of lead in breast milk

Fig. 2 shows the breast milk lead concentrations collected weekly from 16 mothers during days 1–60 postpartum. In the consumption group (n=9), the mean concentration of lead in the breast milk decreased with

Table 1
Demographic characteristics of the subjects

Characteristic	All subjects			Provide weekly breast milk		
	Consumption group (n=35)	Control group (n=37)	p-value	Consumption group (n=9)	Control group (n=7)	p-value
Age (years)	30.8±4.2	31.5±4.0	0.394	33.4±4.3	31.7±1.8	0.364
Height (cm)	160±4.3	159±3.6	0.102	161±3.8	158±3.4	0.105
Weight (kg)						
Before pregnancy	51.5±5.6	52.7±7.5	0.518	53.7±6.8	57.3±3.4	0.397
After pregnancy	65.9±11.0	68.3±7.0	0.414	68.0±8.8	72.5±8.2	0.338
Body mass index (kg/m2)						
Before pregnancy	20.0±1.7	20.8±2.8	0.294	20.7±1.9	23.1±2.9	0.078
After pregnancy	25.6±3.8	27.0±2.7	0.123	26.3±2.6	29.3±2.9	0.059
Neonatal body weight (g)	3099±444	3282±536	0.595	3076±162	2993±227	0.458
Parity						
1	25 (71.4%)	26 (70.3%)	0.914	8 (88.9%)	7 (100%)	<0.001
≥2	10 (28.6%)	11 (29.7%)		1 (11.1%)	0 (0%)	
Drinking during pregnancy						
Yes	1 (2.8%)	0 (0%)	0.300	0 (2.8%)	0 (0%)	0.317
No	34 (97.2%)	37 (100%)		9 (97.2%)	7 (100%)	
Smoking during pregnancy						
Yes	0 (0%)	1 (2.8%)	0.327	0 (0%)	0 (0%)	0.317
No	35 (100%)	36 (97.2%)		9 (100%)	7 (100%)	

Values are given as mean±standard deviation or n (%).

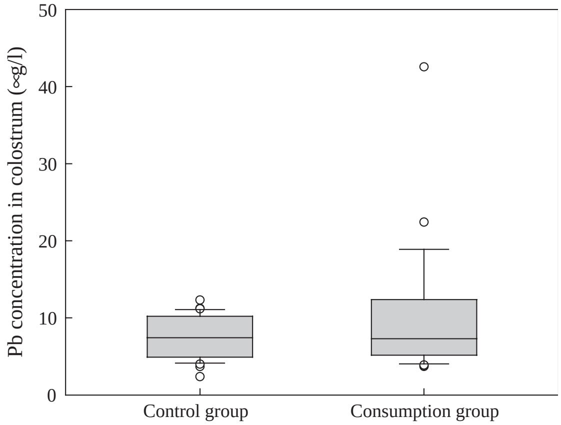

Fig. 1. Box and whisker plots display the distributions of the lead concentrations of colostrum in the consumption (n=35) and control groups (n=37); median (horizontal line in the box), minimum, and maximum are shown. The box includes 50% of the values and is limited by the 25% and 75% percentiles.

days postpartum, from 9.94 µg/L in colostrum to 2.34 µg/L in mature milk. A similar pattern is also found in the control group (n=7, 8.11 µg/L in colostrum, and 2.36 µg/l in mature milk). Lead concentration in breast milk decreases as a function of lactation time. The optimal fits of the breast milk lead concentrations at different lactation stages are presented in Fig. 2, model 1: $C_{\mathrm{m}}(t) = 11.62e^{-0.022t}$ (r^2=0.95, p<0.001) and model

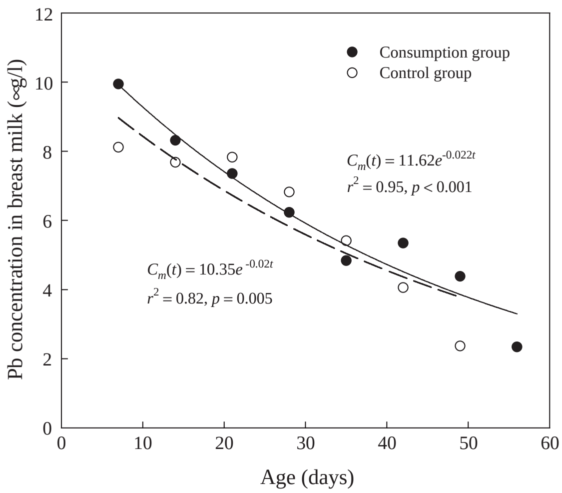

Fig. 2. Optimal model fits of lead concentrations in breast milk at different lactation stages for the consumption and the control groups. The actual data points are shown with symbols (●: consumption group, n=9; ○: control group, n=7); and model fittings are shown in lines (—: consumption group; - -: control group).

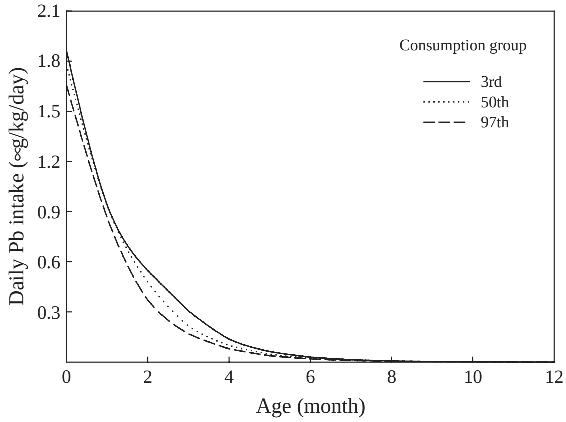

Fig. 3. Estimated daily lead intake by age of breast-fed infants from birth to 12 months.

2: $C_{\mathrm{m}}(t) = 10.35e^{-0.02t}$ (r^2=0.82, p=0.005). The predicted half-life values of lead in breast milk are 32 days and 35 days for the consumption group and the control group, respectively.

3.4. Estimation of daily lead intake and potential health risk of infants

Fig. 3 shows the estimation of daily lead intake of breast feeding infants from birth to 12 months. The daily lead intakes for the consumption group (body weight 3rd, 50th, and 97th percentile) and control group (body weight 3rd, 50th, and 97th percentile) are below the recommended value of Provisional Tolerable Daily Intake (PTDI: 3.57 µg/kg/day). We find the

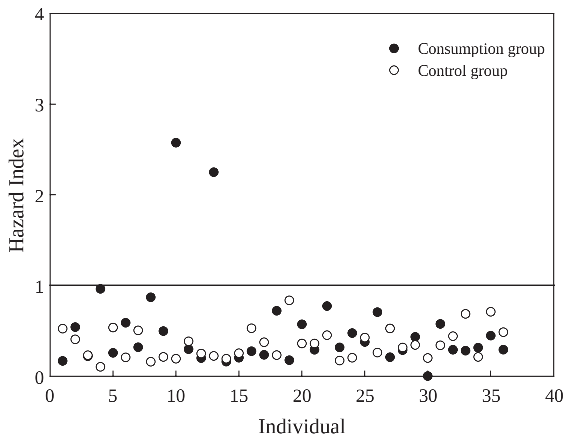

Fig. 4. Individual HI in control group and consumption group. —: Hazard index=1.

higher daily lead intakes in infants at birth and gradually decreasing levels after the first month. Fig. 4 shows the individual lead hazard index of infants in the consumption and control groups. Note that an HI exceeding 1.0 indicates that infant consuming breast milk has a potential health risk. In total, 5.7% (2 out of 35, HI=2.57 and 2.25) of the HI estimates exceed 1.0 for the consumption group.

4. Discussion

In this study, we calculated HI to evaluate the potential health risk of lead in infants. Our results provided essential information regarding the impact of the mother's consumption of traditional Chinese herbs on lead levels in infants fed breast milk. In addition, we found the highest HI in infants at birth.

Lead concentrations in breast milk in our study are comparable to those found in other studies. In Austria, lead concentrations in breast milk were 36±15 μg/L and have decreased continuously since 1993 (Plöckinger et al., 1993). The mean values were 1.63±1.66 μg/L in 2002 (Gundacker et al., 2002). Lead concentrations in breast milk in Italy were 127 μg/L in urban and 46 μg/L in rural areas (Guidi et al., 1992). A study in Sweden reported that lead concentrations in breast milk were 0.7±0.4 μg/L (Hallen et al., 1995). Similar levels were found in Australia (0.73±0.70 μg/kg) (Gulson et al., 1998). In Taiwan, breast milk lead concentrations have decreased as well; the geometric mean (7.68±8.24 μg/L) in our study is much lower than the value (27±29 μg/L) published by Ding et al., (1993). This is most likely due to the policy of Taiwan EPA (Environmental Protection Administration). Taiwan EPA started to promote the use of unleaded fuels in 1987 and prohibited the use of lead fuels completely in 2000.

In our study, lead concentrations in colostrum were 8.59±10.95 μg/L in the consumption group and 6.84±2.68 μg/L in the control group. The higher lead level in the consumption group is due to the consumption of traditional Chinese herbs. Among all herbs, Shy-Wuh-Tang (compound prescription formed by *Rehmaniae radix*, *A. sinensis radix*, *Ligustici rhizoma*, and *Paeoniae radix*) had the highest lead concentration, about 8.8–16.6 times higher than other herbs. Shy-Wuh-Tang is usually used to treat irregular menses, pain during periods, overactive fetus, excessive bleeding during menopause and residual blood clot in uterus after delivery, anemia, and other blood stasis conditions. Because there were no other possible environmental sources of lead in these mothers (e.g. water contamination, occupational exposure, hobbies, use of glazed pottery, or other contaminated kitchenware, etc.), we suggest that reducing the consumption of Shy-Wuh-Tang during pregnancy and lactation may be worth considering.

According to the mathematical models we derived, the predicted half-life values of lead in breast milk are 32 days and 35 days for the consumption group and the control group, respectively. In the early 1990s, Gulson et al. (1998) found that the majority of lead ingested by nursing infants arose from breast milk. As the blood lead level in mother raised, the relative lead concentration in breast milk increased too. Among the breast feeding infants, their breast milk lead correlated very well with their 6-month blood lead (Rabinowitz et al., 1985). Ettinger et al. (2004) showed that infant blood lead at 1 month postpartum was significantly correlated with breast milk (r=0.32, p<0.0001). Our results also indicated that the half-lives of lead in breast milk and in blood ($t_{1/2}$=35 days, Pueschel et al., 1996) were the same.

As a global public health recommendation (WHO, 2002), infants should be exclusively breastfeeding for the first 6 months of life to achieve optimal growth, development, and health. To echo the recommendation, we calculated the daily lead intake from birth to 12 months to present the trends in infants. We found a higher daily lead intake at birth. In Fig. 4, we report two other infants with HI (0.96 and 0.86) near the value of 1. For a single exposure-based assessment, they are unlikely to occur a significant health hazard. But exposure to two or more toxicants may result in additive and/or interactive effects (Hallenbeck, 1993). The PTWI (Provisional Tolerable Weekly Intake) is 50 μg/kg/week for lead for adults. For infants and children, the recommended PTWI is 25 (g/kg/week (PTDI ≈ 3.57 (g/kg/day). This lower intake is recommended because this population is more sensitive than adults to lead. Infants and children also have developing central nervous and immune systems that may make them more sensitive to the adverse effects of contaminated breast milk.

Our study explored the association between mothers' consumption of traditional Chinese herbs and lead body burden in infants in Taiwan. According to our findings, if the mother had consumed traditional Chinese herbs during pregnancy and lactation, it may be worthwhile to monitor the colostrum to protect infants from excessive lead exposure. The quality of raw material for traditional Chinese herbs may be affected by environmental contaminants and cultivated materials, so there should be frequent monitoring of purity. In conclusion, the consumptions of traditional Chinese herbs by the mothers in this study significantly affected the body burden of lead in their infants.

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